UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,043	10/25/2000	Eino Elias Hakalehto	933-162P	3800

2292 7590 03/29/2002

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/29/2002 18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/646,043	Applicant(s) HAKALEHTO, EINO ELIAS	
	Examiner Khatol S Shahnan-Shah	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment C received January 7, 2002, paper 17 is acknowledged. Claims 1-13 were canceled without prejudice. New claims 14-26 were added.

2. Claims 14-26 are pending and under consideration.

Prior Citations of Title 35 Sections

3. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Objections Maintained

4. Objection made in paragraph 4 of the office action mailed 7/05/2001, paper # 15 is maintained. Applicant's response of January 7, 2002 mentions an Abstract of Disclosure located on a separate sheet attached to said response, however the office did not received said attachment.

5. Objection to the drawings made in paragraph 5 of the office action mailed 7/05/2001, paper # 15 by the Draftsperson is maintained. No corrected drawings have been submitted.

Objections Withdrawn

6. Objection to the drawings made in paragraphs 6 and 8 of the office action mailed 7/05/2001, paper # 15 is withdrawn in view of applicant's amendment.

7. Objection to the priority made in paragraph 7 of the office action mailed 7/05/2001, paper # 15 is withdrawn in view of applicant's amendment.

Rejections Moot

8. Rejection of claims 1-2 and 11 made under 35 USC 112-first paragraph in paragraph 9 of the office action mailed 7/05/2001, paper # 15 is moot in view of applicant's cancellation of the claims.

9. Rejection of claims 1-2 made under 35 USC 112-second paragraph in paragraph 10 of the office action mailed 7/05/2001, paper # 15 is moot in view of applicant's cancellation of the claims.

10. Rejections of claim 7 made under 35 USC 102(b) in paragraphs 11, 12 and 13 of the office action mailed 7/05/2001, paper # 15 is moot in view of applicant's cancellation of the claims.

11. Rejections of claim 7 made under 35 USC 102(b) in paragraphs 14 and 15 of the office action mailed 7/05/2001, paper # 15 is moot in view of applicant's cancellation of the claims.

New Claim Objections

12. Claim 20 is objected to because of the following informalities:

The claim recites a peptide sequence, which is not identified by a SEQ ID Number. Appropriate correction is required.

New Grounds for rejections

Claim Rejections - 35 USC § 112- first paragraph

13. Claims 14-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting *Salmonella* species from a cultivation medium, does not reasonably provide enablement for <u>all</u> bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims recite a method for detecting bacteria from a cultivation medium by detecting antigens, which are, expressed soon after inoculation, which encompasses any bacteria and any microbial antigen. However, the specification is directed towards detecting *Salmonella* in foodstuff. (see page 3) The specification mainly mentions two strains *Salmonella typhimurium* and *Salmonella enteriditis* that are the cause of food-borne disease (page 6). In example 4 specification recites the use of RVS broth as growth medium (page 4, line 9). In the same line it is mentioned that the plate cultures were started simultaneously with ELISA measurements, it's not clear which medium was used to plate the organism and how bacterial densities were measured. The specification fails to provide essential information and steps. There is not enough guidance in regard to the production of antibodies against different fimbrial antigens of other bacteria or other enteric bacteria and their similarity or differences with the *Salmonella.*

It is well known in the art that fimbriae are thin, proteinaceous, polymeric surface organelles expressed by the members of Enterobacteriaceae including most *Salmonellas*. The adhesive function of Particular fimbriae of *E.coli* has been well studied. However the role of *Salmonella* fimbriae is not well understood (Dibb-Fuller, Letters in Applied Microbiology 1997. Prior art already made of record). There are many different fimbriae known to be expressed by *Salmonella*, (i.e. SEF 14, 17, 21 etc) (Dibb-Fuller page 451). Also, little information is available on the *invitro* conditions of expression of these fimbriae (Dibb-Fuller page 447).

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the court of appeals in In re Wands, 8 USPQ 2d 1400 at 1404 (CAFC 1988).

These factors include 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, and 8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other bacteria and their antigens having the claimed functional feature of *Salmonella* fimbrial antigens, 3) there are no working examples which suggest the desired results can be obtained in other bacteria, 4) the nature of the invention involves the complex and incompletely understood area of rapid detection methods, 5) the state of the prior art shows the lack of correlates to bacterial fimbrial antigens, 6) the relative skill of those in the art is commonly recognized as quite high (post – doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

Claim 20 of the instant application is not only drawn to a synthetic polypeptide but is also drawn to a derivative thereof. The specification discloses an 18 amino acids sequence (SEQ ID #1 (see amended A). The amended specification recites that this sequence was traced from the *Salmonella typhimurium* type 1 fimbriae and in order to select a specific sequence differing from the corresponding *E. coli* type 1 fimbriae, the two sequences were compared with each other. There is no guidance provided as to how different these sequences were from each other.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein or a peptide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of prediction protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is **not** routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. Multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claim 20, which encompass all modifications and fragments because the specification does **not** disclose the following:

- an amino acid sequence for the claimed protein;
- the general tolerance to modification and extent of such tolerance;
- specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which retain the biological activity if the intact protein; and
- the specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicant have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen Inc v. Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed.Cir.1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S.P.Q. 546(Bd. Pat. App. & Int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the invention commensurate in

scope with the claims.

Claim Rejections - 35 USC § 112-second paragraph

14. Claims 14-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitation "detecting antigens which are expressed soon after inoculation". It is not clear what time period between 3 to 10 hours constitutes this phase.

Claim 14 recites the limitation "before actual growth phase". It is not clear what time period between 3 to 10 hours constitutes this phase.

Claim 14 recites the limitation "in the beginning of the growth phase". It is not clear what time period between 3 to 10 hours constitutes this phase.

Claim Rejections - 35 USC § 102

15. Claims 14-17 and 21-26 are rejected under U.S.C. 102(b) as being anticipated by Van Pocket, L.S.G. (Applied and Environmental Microbiology, Vol. 56, No. 4, pp. 924-927, 1990).

Claims are drawn to a method for detecting bacteria within a time period of 3 to 10 hours by detecting antigens which are detected soon after inoculation into the medium.

Van Poucke teach a method for detecting bacteria within a time period of 4 to 8 hours by detecting antigens which are detected soon after inoculation into the medium (see page 925).

Van Poucke also teach a method wherein bacterial antigens are detected immunologically using antibodies. They use a micro-ELISA assay (*Salmonella*- TEK). (see abstract and page 925). Van Poucke teaches that the detected bacteria are coliform enteric bacteria belong to genus

salmonella. Van Poucke also teaches temperatures of about 37 °C and above 42 °C. (see page 925). The prior art teaches the claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 14-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Poucke, L.S.G. (Applied and Environmental Microbiology, Vol. 56, No. 4, pp. 924-927, 1990) in view of Thorns, C. J. et al. (US Patent Number 5,510,241). Prior art already made of record.

Claims are drawn to a method for detecting bacteria within a time period of 3 to 10 hours by detecting antigens which are detected soon after inoculation into the medium.

Van Poucke teach a method for detecting bacteria within a time period of 4 to 8 hours by detecting antigens which are detected soon after inoculation into the medium (see page 925).

Van Poucke also teach a method wherein bacterial antigens are detected immunologically using antibodies. They use a micro-ELISA assay (*Salmonella*- TEK). (see abstract and page 925). Van Poucke teaches that the detected bacteria are coliform enteric bacteria belong to genus *salmonella*. Van Poucke also teaches temperatures of about 37 °C and above 42 °C. (see page 925). Van Poucke does not teach fimbrial proteins. However, Thorn et al. teach a method for testing for the presence of *Salmonella* species expressing fimbrial antigens, which have been grown on a selected medium. (see title and abstract and claims). They used a variety of liquid and solid media (see column 2, lines 25-65) and various temperature ranges from 22°C to 60° C

(see columns 5 and 6). They also used direct binding and indirect ELISA methods. They too teach a method wherein the microbial antigens are detected with antibodies, which have been produced against synthetic peptides or a derivative thereof (see column 11 and claims). They also teach derivatives of the claimed synthetic peptide (see SEQ ID # 1, (i.e. amino acid 165-167) columns 26-28).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the rapid method of screening taught by Van Poucke and the method taught by Thorn et al. to obtain the instant disclosure. Given the fact that rapid screening methods for *Salmonella* are needed. One having ordinary skill in the art would have been motivated by expectation of success and the attainment of a better method to obtain a method which shortens the cultivation period for detecting bacteria such as *Salmonella* which are a major cause of food poisoning. New approaches should be rapid, so that results can be obtained and appropriate action can be taken within a shorter period.

Conclusion

17. No claims are allowed.

18. THIS ACTION IS MADE FINAL necessitated by applicants' amendments. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

3/20/02

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600